Marchenko et al., J. Biol. Chem. 275(2000):16202-16212). There is evidence from mutation analysis that the transcription activation functions of p53 responsible for growth arrest and apoptosis can be dissected. For example, the p53 Q22/S23-mutant protein has abrogated growth arrest function but only attenuated apoptosis induction capacity (Venot et al., Oncogene 18(1999):2405-2410). On the other hand, several p53 amino acid 175 mutants were identified that retain cell cycle arrest function but are impaired in apoptosis induction (Ryan and Vousden, Mol. Cell. Biol. 18(1998):3692-3698). Furthermore, several p53 homologues have been identified, including p73 and p63, which share part of the functions with p53 (Kaghad et al., Cell 90(1997):809-819; Yang et al., Mol. Cell 2(1998):305-316). In the presence of the adenovirus E1B-19kDa protein, which binds to and inactivates pro-apoptotic death genes of the *bcl-2* family, the p53-dependent growth arrest pathway becomes apparent. Otherwise, apoptosis is dominant over growth arrest (Han et al., Genes Dev. 10(1996):461-477).

Recombinant adenoviruses, are finding increasing utility for the treatment of cancer and other diseases involving inappropriate cell survival. In particular, CRAds have been developed to selectively replicate in and kill cancer cells. Such cancer-specific CRAds represent a novel and very promising class of anticancer agents (reviewed by Heise and Kirn, *supra*, Alemany et al., *supra*; Gomez-Navarro and Curiel, *supra*). The tumor-selective replication of this type of CRAds is achieved through either of two alternative strategies. In the first strategy, the expression of an essential early adenovirus gene is controlled by a tumor-specific promoter (Rodriguez et al., Cancer Res. 57(1997):2559-2563; Hallenbeck et al., Hum. Gene Ther. 10(1999):1721-1733). The second strategy involves the introduction of mutations in viral genes to abrogate the interaction of the encoded proteins with cellular proteins, necessary to complete the viral life cycle in normal cells, but not in tumor cells (Bischoff et al., Science 274(1996):373-376; Fueyo et al., Oncogene 19(2000):2-12; Heise et al., Clin. Cancer Res. 6(2000):4908-4914; Shen et al., J. Virol. 75(2001:4297-4307). During their replication in tumor cells CRAds destroy these cells by inducing lysis, a process that is further referred to as "oncolysis". The release of viral progeny from lysed tumor cells offers the potential to amplify CRAds

C L A I M S

1. Replication competent recombinant adenovirus, being capable to replicate and having lytic capacity in target cells, the said cells being hampered in the p53 dependent apoptosis pathway, the virus comprising in the genome thereof, the coding sequence of at least one restoring factor functional in restoring the p53 apoptosis pathway in the said target cells, operably linked to one or more expression control sequences, functional in the said target cells.

2. Recombinant virus according to claim 1, wherein the virus is a human adenovirus, preferably of serotype 5.

3. Recombinant virus according to claim 1 or 2, wherein the adenovirus is a conditionally replicating adenovirus.

4. Recombinant virus according to claim 1 or 2, wherein the adenovirus is a heterologously trans-complemented adenovirus.

5. Recombinant virus according to any of the preceding claims, wherein the virus genome comprises at least the gene encoding the adenovirus E1B-55kDa protein or a functional analogue or derivative thereof.

6. Recombinant virus according to claim 5, wherein the virus genome further comprises the gene encoding the adenovirus E1B-19kDa protein or a functional analogue or derivative thereof.

7. Recombinant virus according to claim 5 or 6, wherein the virus genome comprises one or more, preferably all, of the genes of the adenovirus E4 region encoding E4 proteins or functional analogues or derivatives thereof.

8. Recombinant virus according to claim 7, wherein the virus genome comprises at least the gene encoding the adenovirus E4orf6 protein or a functional analogue or derivative thereof.

9. Recombinant virus according to any of the preceding claims, wherein the adenovirus carries a mutation in the E1A region encompassing at least a part of the pRb-binding CR2 domain of E1A, preferably a deletion encompassing amino acids 122 to 129 (LTCHEAGF) of E1A.

10. Recombinant virus according to any of the preceding claims wherein the restoring factor is chosen from the group, consisting of p53, p63, p73, BAX, BAK, BOK/Mtd, BCL-X_S, Noxa/APR, PIDD, p53AIP1, PUMA,KILLER/DR5, Apaf-1, PIG, BID, tBID, BAD, HRK, Bik/Nbk, BLK, mda-7, p14ARF or a functional variant, analogue or derivative thereof.

11. Recombinant virus according to claim 10, wherein the restoring factor is p53 protein, preferably human p53, or a functional analogue or derivative thereof.

12. Recombinant virus according to claim 11, wherein the protein lacks a functional binding domain for the human MDM2 protein.

13. Recombinant virus according to claim 11 or 12, wherein the protein is a functional derivative of human p53 with mutated amino acids Leu-14 and Phe-19.

14. Recombinant virus according to any of the preceding claims, wherein the target cell is a human cell, preferably chosen from the group, consisting of cancer cells, arthritic cells, hyperproliferative vascular smooth muscle cells and cells infected with a virus other than the said recombinant virus.

15. Use of the recombinant virus according to any of the claims 1-14 in a medicament.

16. Use according to claim 15 for the manufacture of a medicament for suppressing uncontrolled cell growth, in particular malignant cell growth.

17. Method for lysing target cells hampered in the p53 dependent apoptosis pathway, comprising the steps of:

- infecting the said target cells with a virus, having lytic capacity in the said target cells,

- replicating the said virus within the said target cells, further comprising the step of providing, in the virus genome the coding sequence of at least one restoring factor, functional in restoring the p53 dependent apoptosis pathway, the said coding sequence being capable to be expressed in the target cells upon infection thereof by the said virus.

18. Method according to claim 17, wherein the target cells are infected by a recombinant virus according to any of the claims 1-14.

19. Method according to claim 17 or 18, further comprising the step of subjecting said target cells to irradiation and/or a toxic chemical compound.

20. Method according to any of the claims 17-19, wherein said target cells are present in an animal body, preferably a human body.

21. Method for treatment of a subject body suffering from a condition involving body cells hampered in the p53 dependent apoptosis pathway, comprising the step of administering to the said subject body an effective amount of the recombinant virus according to any of the claims 1-14.

22. Method according to claim 21, wherein the condition is associated with uncontrolled cell growth.

23. Method according to claim 22, wherein the condition is chosen from the group, consisting of cancer, arthritis, in particular rheumatoid arthritis, or vascular smooth muscle cell hyperplasia.